

## AMENDMENTS

### IN THE CLAIMS

Please cancel claims 12-17 and amend claims 1-4, 8, 9, 11, 18-20, and 22-28 and add new claims 29-34 as shown below.

1. (Currently Amended) A standardized prion preparation, comprising:  
prions obtained from a plurality of ~~animals~~ transgenic mouse brains; and  
a carrier;

wherein the preparation comprises ~~is characterized by containing~~ prions (a) which infect and cause disease in an animal chosen from a human, a cow, and a sheep ~~a known species of animal~~, (b) which are prions of a known strain, and ~~(c) which are present in a known amount, and~~ further wherein the carrier is ~~of a known composition which is~~ different from brain tissue of the animal chosen from a human, a cow and a sheep ~~mammal which the prions would infect in the animals natural state.~~

2. (Currently Amended) The preparation of claim 1, wherein the prions are present in ~~known amount~~ is a known number of infectious units and a known concentration of prions ~~and wherein the known species is selected from the group consisting of human, cow and sheep.~~

3. (Currently Amended) The preparation of claim 1, wherein the preparation is a comprised essentially of transgenic mouse brain homogenate, ~~the carrier is comprised of brain tissue from a mouse and wherein the prions infect and cause disease in a mammal selected from the group consisting of human, cow and sheep.~~

4. (Currently Amended) The preparation of claim 1, wherein the prions ~~substantially all prions present in the preparation~~ are of a single strain ~~and wherein the carrier is comprised of water.~~

5. (Original) The preparation of claim 4, wherein the strain has a polymorphism selected from the group consisting of: human M129, human V129, human E219, human K219, sheep R171,

sheep E171, sheep A136, sheep V136, a bovine 5 octarepeat polymorphism, and bovine 6 octarepeat polymorphism.

6. (Original) The preparation of claim 4, wherein the strain is human and has a pathogenic mutation selected from the group consisting of: a 2 octarepeat insert, a 4 octarepeat insert, a 5 octarepeat insert, a 6 octarepeat insert, a 7 octarepeat insert, an 8 octarepeat insert, a 9 octarepeat insert, P102L, P105L, A117V, D178N, V180I, F198S, E200K, V210I, D217R, M232A, and a stop codon at 145.

7. (Original) The preparation of claim 1, wherein the prions are of a plurality of different known strains and wherein the prions are obtained from 10 or more animals, and further wherein the prions are produced in a transgenic mouse having a genome comprising exogenous genetic material encoding at least a portion of a PrP protein.

8. (Currently Amended) The preparation of claim 1, wherein the prions are obtained from a mouse having an ablated endogenous PrP gene and a genome manipulated to express a high copy number of an exogenous PrP gene from a genetically diverse animal chosen from a human, a cow and a sheep, and wherein the mouse spontaneously forms prions that normally infect the genetically diverse animal ~~wherein the genetically diverse animal is selected from the groups consisting of a human, cow, sheep, dog, cat, goat, chicken or turkey.~~

9. (Currently Amended) The preparation of claim 1, wherein the prions are uniformly dispersed in the preparation and are produced in a transgenic mouse selected from the group consisting of: Tg(HuPrP), Tg(HuPrP)/Prnp<sup>+/-</sup>, Tg(HuPrP)/Prnp<sup>0/0</sup>, Tg(HuPrP<sup>CJD</sup>), Tg(HuPrP<sup>CJD</sup>)/Prnp<sup>+/-</sup>, Tg(HuPrP<sup>CJD</sup>)/Prnp<sup>0/0</sup>, ~~Tg(SHaPrP), Tg(SHaPrP<sup>+/-</sup>), Tg(SHaPrP<sup>+/-</sup>)/Prnp<sup>+/-</sup>, Tg(SHaPrP<sup>+/-</sup>)/Prnp<sup>0/0</sup>, Tg(SHaPrP)/Prnp<sup>+/-</sup>, Tg(SHaPrP)/Prnp<sup>0/0</sup>, Tg(ShePrP), Tg(ShePrP)/Prnp<sup>+/-</sup>, Tg(ShePrP)/Prnp<sup>0/0</sup>, Tg(BovPrP), Tg(BovPrP)/Prnp<sup>+/-</sup>, and Tg(BovPrP)/Prnp<sup>0/0</sup>.~~

10. (Original) The preparation of claim 1, produced in a transgenic mouse selected from the group consisting of: Tg(MHu2M), Tg(MHu2M)/Prnp<sup>+/-</sup>, and Tg(MHu2M)/Prnp<sup>0/0</sup>.

11. (Currently Amended) A prion protein standard composition comprising:  
isolated exogenous prions from a plurality of transgenic mice genetically manipulated  
to allow infection by prions that normally only infect a genetically diverse animal chosen from a human,  
a cow and a sheep, said mice being infected with prions of the genetically diverse animal; and  
brain homogenate ~~from the genetically diverse animal~~;  
wherein the standard composition has properties chosen from a known endogenous  
host prion protein concentration, a known number of infectious units, a known exogenous host prion  
protein concentration, a known endogenous prion protein from the genetically diverse animal, a known  
sensitivity for an antibody, and a known background protein concentration, sufficiently established to  
serve as reference control for prion measurement protocols chosen from calibration of an apparatus,  
calibration of an assay, determination of specificity of an assay, determination of sensitivity of an assay,  
and determination of quality of an assay reagent.

12. (Canceled)

13. (Canceled)

14. (Canceled)

15. (Canceled)

16. (Canceled)

17. (Canceled)

18. (Currently Amended) The preparation of claim 1, comprising method of claim 17,  
~~wherein the known amount of prions of the homogenized prion preparation is a known number of  
infectious units, and wherein the number of infectious units is between 0.1 and about 100~~ infectious  
units of prions.

19. (Currently Amended) The preparation of claim 1, comprising between about 1 and about 10 infectious units of prions ~~and wherein the transgenic host animals are mice and the genetically diverse animal is selected from the group consisting of: a human, cow, sheep, dog, cat, goat, chicken or turkey.~~
20. (Currently Amended) A method of calibration of a prion protein assay, comprising the steps of:
- providing a prion protein standard comprising prions which infect and cause disease in an animal chosen from a human, a cow and a sheep;
  - determining a ~~true~~ an actual value of prion protein concentration in the prion standard;
  - subjecting a portion of the preparation to prion protein assays to determine an assay value for the standard;
  - determining a correction value for the assay based on the ~~true~~ actual value; and
  - adjusting the assay value to reflect the ~~true level~~ actual value of prion protein in the standard;
  - wherein the assay is calibrated by adjusting the assay value to reflect the ~~true~~ actual value of prion protein concentration in a sample.
21. (Original) The method of claim 20, wherein the assay is calibrated using a plurality of standards with different prion protein concentrations.
22. (Currently Amended) The method of claim 20, further comprising the steps of:
- subjecting a portion of the preparation to a second prion protein assay to determine a second assay value for the standard;
  - determining a correction value for the second assay based on the ~~true~~ actual value; and
  - adjusting the second assay to reflect the ~~true level~~ actual value of prion protein in the standard; and
  - comparing the adjusted levels of prion protein in each assay;
  - wherein the assays are calibrated with respect to one another by adjusting the assay values detected by each assay to reflect the ~~true~~ actual values of prion protein concentration.

23. (Currently Amended) A prion protein standard kit, comprising a plurality of protein preparations, each preparation ~~comprising~~ characterized by containing prions (a) which infect and cause disease in a known species of mammal chosen from a human, a cow and a sheep, (b) which are of a known strain, (c) which are present in a known ~~amount~~ number of infectious units, and, (d) which are obtained from a plurality of ~~animals~~ transgenic mice.

24. (Currently Amended) The kit of claim 23, wherein each preparation ~~contains~~ consists of a different ~~amount~~ number of infectious units of prions ~~characterized by the ability to infect and which~~ cause disease in ~~the same~~ a single species.

25. (Currently Amended) [A] The kit of claim 23, wherein each preparation ~~contains~~ consists of a different ~~amount~~ number of infectious units of a single strain of prion.

26. (Currently Amended) The kit of claim 23, wherein each preparation ~~has a same known amount of~~ consists of a different prion strain.

27. (Currently Amended) The kit of claim 26, wherein each prion strain is ~~characterized by the ability to infect and causes~~ disease in a different species.

28. (Currently Amended) The kit of claim 26, wherein each preparation ~~has~~ consists of one infectious unit of prions.

29. (New) The preparation of claim 1, wherein the transgenic mouse brains are obtained from a transgenic mouse having both endogenous PrP genes ablated.

30. (New) The preparation of claim 29, wherein the prions infect and cause disease in a cow.

31. (New) The preparation as claimed in claim 1, wherein the prions infect and cause disease in a human.

32. (New) The preparation of claim 1, wherein the transgenic mouse brains are produced in transgenic mice which are Tg(BovPrP)/Prnp<sup>0/0</sup>.
33. (New) A standardized prion preparation, comprising:  
prions obtained from a plurality of mice which are Tg (BovPrP)Prnp<sup>0/0</sup>; and  
a carrier;  
wherein the prions infect and cause disease in a cow and are prions of a known strain.
34. (New) The preparation of claim 33, comprising a known number of infectious units.